

## R E M A R K S

### A. Summary of the Invention

Broadly, in one aspect, the present invention concerns a method of determining the identity of one or more nucleotide basis at a plurality of specific positions in one or more nucleic acid molecules of interest. The method includes the step of treating a sample comprising the nucleic acid molecules of interest if the nucleic acid molecules are double stranded so as to obtain unpaired nucleotide bases spanning the specific positions. Alternatively, a sample of the nucleic acid of interest may be used directly if the nucleic acid molecules are single stranded. The method of the invention includes the step of contacting the sample with a plurality of different oligonucleotide primers. Each different oligonucleotide primer hybridizes under high stringency hybridization conditions to a corresponding different stretch of nucleotide bases present in the nucleic acid molecules of interest which is immediately adjacent to the specific position of a nucleotide base to be identified with that oligonucleotide primer, so as to form a duplex such that the nucleotide base to be identified is the first unpaired base of the nucleic acid molecule of interest immediately downstream of the 3' end of the primer. Each different oligonucleotide primer comprises a corresponding different affinity moiety. The oligonucleotide primer comprising the affinity moiety is capable of hybridizing with a nucleic acid template and undergoing a nucleic acid template-dependent primer extension reaction with terminator of a terminator reagent. The affinity moiety permits affinity separation of the extended oligonucleotide primer from the terminator reagent. The method of the invention includes the further step of contacting the duplexes with a terminator reagent which includes four different terminators of a nucleic acid template dependent primer extension reaction. The terminator reagent is free of dATP, dCTP, dGTP, and dTTP. Each terminator comprises a different detectable label corresponding to the terminator. One of the terminators is complementary to a nucleotide base to be identified by each of the oligonucleotide primers. The contacting is carried out in a primer extension reaction medium under conditions sufficient to permit a template dependent primer extension reaction, which incorporates the complimentary terminator onto the 3' end of each of the different oligonucleotide primers to thereby extend the 3' end of each of the

primers by one terminator. The method of the invention further includes the step of affinity separating the respective extended oligonucleotide primers from the primer extension reaction medium by causing each of the extended oligonucleotide primers to contact an affinity group attached to a solid support. The affinity group is complementary to the affinity moiety incorporated in the oligonucleotide primer. Finally, the method of the invention includes the step of determining the presence and identity of the nucleotide base at each of the respective specific positions in the one or more nucleic acid molecules of interest by detecting the detectable label of the terminator incorporated at the 3' end of each of the affinity separated extended oligonucleotide primers.

B. Summary of the Outstanding Office Action

The attorneys for the applicants note with appreciation that claims 64 and 66 through 71 inclusive were allowed in the Office Action of 12 May 2003.

In the outstanding Office Action, claims 60 through 63 inclusive and 65 of the subject application were finally rejected under 35 USC §112, first paragraph, with the assertion that the claims contained subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Claims 60 through 63 inclusive and 65 were finally rejected in the Office Action of 12 May 2003 under 35 USC §112, second paragraph with the assertion that the claims were indefinite for assertedly failing to particularly point out and distinctly claim subject matter which the applicants regarded as the invention

C. Summary of the Present Amendments  
and Request for Reconsideration

Although the attorneys for the applicants maintain their position that claims 60 through 63 inclusive and 65 of the subject application fully meet the standards of 35 USC §112, first and second paragraphs for the reasons set forth in a previous reply dated 24 March 2003, in order to

Applicants: GOELET, Philip *et al.*  
Application No.: 09/258,132  
Filing Date: 26 February 1999  
Page 8

expedite prosecution of the subject application, claims 60 through 63 inclusive and 65 have been cancelled without prejudice in the present reply after final action. The applicants expressly reserve the right to prosecute claims directed to the subject matter of any of cancelled claims 60 through 63 inclusive and 65 in one or more continuation, divisional, or other continuing patent application.

Reconsideration of the subject application as amended above is respectfully requested.

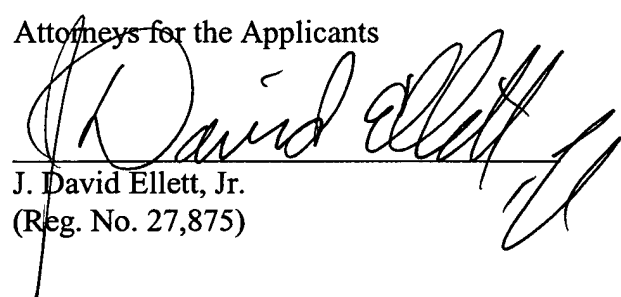
D. Conclusion

Since the claims remaining in the subject application, claims 64 and 66 through 71 inclusive, were allowed in the Office Action of 12 May 2003, it is submitted that the application is now in condition for allowance. Such action is therefore earnestly solicited.

Respectfully submitted,

Attorneys for the Applicants

by:

  
J. David Ellett, Jr.  
(Reg. No. 27,875)

Telephone No. (212) 813-1600